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Combined Use of Beta-Adrenergic Blocking Agents and Long-Term Cardiac Pacing for Patients With the Long QT Syndrome

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Objective. **The objective of this study was to review our current experience using a combination of beta-adrenergic blocking agents and long-term cardiac pacing to treat patients with the idiopathic long QT syndrome.**

Background. **Patients with the idiopathic long QT syndrome are at high risk for sudden cardiac death. Before combination therapy, 20 of the 21 study patients experienced either cardiac arrest (n = 8) or syncope (n = 18) and 11 had documented polymorphous ventricular tachycardia. Nine of these patients had not responded to isolated beta-blocker therapy and five had not responded to isolated left cervicothoracic sympathectomy.**

Method. **All patients were treated with combined beta-blocker therapy and long-term cardiac pacing at a rate designed to normalize the QT interval.**

Results. **Cardiac pacing at rates of 70 to 125 beats/min resulted in shortening of the QT and corrected QT (QTc) intervals from 517 ± 76 and 541 ± 62 ms to 404 ± 37 and 479 ± 41 ms, respectively. The mean follow-up interval after institution of pacing was 55 ± 45 months. The only sudden death occurred in a patient who had discontinued beta-blocker therapy. Syncope occurred in four patients, two of whom had interrupted pacemaker function due to lead fracture. Pacemaker problems, partly attributable to the specific rate required for QT interval shortening and to avoidance of T wave sensing, were relatively common. No patient who continued the combination therapy died, but 10% of these patients had a recurrence of symptoms.**

Conclusions. **Combination therapy with a beta-blocker and cardiac pacing appears to be a highly effective primary therapy for symptomatic patients with the long QT syndrome and to provide excellent adjunctive therapy for patients who require insertion of an automatic internal defibrillator.**

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The relation between sudden cardiac death and cardiac arrhythmias in patients with the long QT syndrome was first described by Fraser et al. (1). In that study and in subsequent reports, the relation between bradycardia and the long QT syndrome was reported (2). Bradycardia may be related to abnormal sympathetic activation of the heart (3). In 1987, we (2) described the combined use of beta-adrenergic blocking agents and long-term cardiac pacing in the treatment of patients with the long QT syndrome with or without bradycardia. In that study, we reported on eight patients who responded to such combination therapy over a relatively short follow-up interval after traditional therapy had proved unsuccessful. The combination therapy was designed to prevent both pauses and increased adrenergic tone, either of which might trigger episodes of polymorphous ventricular tachycardia. Since the initial report, we have used combination therapy for all symptomatic patients with the long QT syndrome referred to our medical center. In this report we update our current experience, emphasizing the benefits and potential problems with this approach.

Methods

This report includes follow-up information on the 8 patients with the long QT syndrome previously reported on and an additional 13 patients who have received combination therapy since the original report. The clinical data for these patients are detailed in Table 1. All but one patient was symptomatic and had consistent prolongation of the QT interval to >440 ms and a corrected QT (QTc) interval >450 ms unrelated to any identifiable cause. Baseline evaluation included an echocardiogram in all patients and exercise treadmill testing in all but Patient 19. No patient had evidence of cardiac disease, and the QT interval shortened in all patients in response to treadmill exercise (2). The results of tilt table testing, performed in four patients (Patients 10, 13, 14 and 18), were normal.

Patients were treated with maximal tolerated doses of one or more beta-blockers and insertion of a cardiac pacemaker. The pacemaker rate was adjusted to the minimal rate required to normalize the QT interval. The exact pacing mode and beta-blocker dose used are detailed in Table 2. Family members with a prolonged QT interval but without symp-

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Table 1. Clinical Characteristics of the Study Patients

Pt No.	Age (yr)/ Gender	Family History*	Syncopal Episodes	Episodes of ASD	Duration of Symptoms (mo)	Documented PMVT	AVB
1	39/F		10		84	+	
2	38/F		5	1	72	+	+
3	22/F	+	>20	4	48	+	+
4	39/F	+ †	>20		324	+	
5	30/F		7		72		
6	25/F	+	>10	2	60	+	
7	30/F	+	8		180	+	+
8	63/F	+	>40		588		
9	51/M		1		1		
10	20/F		1		1	+	
11	55/F			1	1		
12	31/F		7		60		
13	18/F	+		1	1		
14	29/F		1	1	48	+	
15	42/F	+	6		240		
16	12/M	+	5		24		
17	13/M	+	1	2	108	+	
18	13/F	+	4		18		
19	2/F		>20	1	1	+	+
20	16/F		>20		72	+	
21	13/M	+			0		+

*Family history of recurrent syncope or aborted sudden death, or both; †Patient 4 is the mother of Patient 13. Patient 8 is the grandmother of siblings Patient 3 and Patient 21, and Patient 15 is the mother of Patient 17. + = present. ASD = aborted sudden death; AVB = atrioventricular block; F = female; M = male; PMVT = polymorphous ventricular tachycardia; Pt = patient.

toms were treated with beta-blockers; those with a normal QT interval were not treated.

The baseline QT and QTc intervals were prolonged in all except Patient 13, who was resuscitated from cardiac arrest and who is the daughter of Patient 4. Atrial demand pacing (AAI) was initiated in eight patients; in one of these (Patient 3), the pacemaker was upgraded to a dual-chamber system (DDD). Since July 1989, all patients have received either a ventricular demand (VVI) or a dual-chamber (DDD) pacemaker. In one (Patient 15), the pacemaker was later programmed to AAI mode.

Ethics of the study. Combined beta-blocker therapy and chronic pacing has become one of the standard modes of therapy for patients with the long QT syndrome. Our study was a descriptive prospective study of patients under our care. The study design in no way interfered with standard care.

Patient follow-up. The patients were followed up at least every 6 months either at our arrhythmia clinic or by the referring physician. If symptoms recurred, intensive efforts were made to discern their cause. In addition, all patients underwent regular pacemaker evaluation and 24-h ambulatory electrocardiographic (ECG) monitoring as clinically indicated. Twelve-lead ECGs were obtained at these times to document persistent normalization of the QT interval. All but three patients were followed up at the University of California, San Francisco Medical Center. Follow-up data from two patients included in our original report were obtained from the referring physicians at their respective institutions (the University of Minnesota and the University of Southern California). One patient currently resides in Hawaii and is followed up there. All except Patient 21 were followed up for a minimum of 6 months.

Results

Clinical features. The study group consisted of 21 patients, 17 women and 4 men, aged 2 to 63 years (mean 28 ± 15). Ten patients were from six families with the Romano-Ward syndrome and one patient had the Jervell-Lange-Nielsen syndrome. Eight patients had a history of one to four episodes of resuscitation from sudden cardiac arrest. One asymptomatic relative with QT interval prolongation received combined therapy because of spontaneous atrioventricular (AV) block and ventricular ectopic activity in association with a family history of sudden cardiac death. Eighteen patients had a history of one or more syncopal episodes and 11 had documented polymorphous ventricular tachycardia. Five of the 21 patients had episodes of AV block but none had bradyarrhythmias.

Unsuccessful prior therapy is detailed in Table 2. Nine patients did not respond to trials of selective and nonselective beta-adrenergic blocking agents. Labetalol, which has both beta- and alpha-adrenergic blocking effects, was not

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Table 2. Therapy and Follow-Up of Patients

Pt No.	Unsuccessful Therapy	Baseline QT (ms)	Baseline QTc (ms)	Pacemaker Mode	Pacemaker Rate (beats/min)	Postpacing QT (ms)	Postpacing QTc (ms)	Follow-Up (mo)*	Events
1	Propranolol 80 mg; phenytoin; LCTS	480	453	AAI	85	400	476	106	
2	Nadolol 120 mg; atenolol 100 mg; LCTS	480	453	AAI	85	360	428	92	Syncope, AICD
3	Propranolol 120 mg; phenytoin; LCTS	580	552	AAI/DDD	80	440	530	122	Syncope†
4	Propranolol 120 mg; phenytoin; LCTS	500	538	AAI	70	420	457	156	
5	Nadolol 120 mg	520	565	DDD	80	420	506	84	
6	Phenobarbital	560	528	VVI	75	410	455	97	
7	Phenytoin	560	502	VVI	80	460	552	115	
8	Phenytoin	520	520	AAI	85	400	476	72	
9		640	560	DDD	85	400	476	25	Pacemaker syndrome
10	LCTS	447	510	VVI/DDD	100	400	519	24	Syncope, PMVT
11		470	594	DDD	75	460	517	35	
12	Atenolol 100 mg	640	697	AAI	75	350	390	29	
13		360	439	DDD	85	380	452	22	
14	Atenolol 100 mg	520	565	AAI	70	440	478	24	
15		440	500	DDD	80	380	437	10	
16		540	628	DDD/AAI	80	360	430	15	
17		590	590	DDD	90	440	543	19	
18		460	474	DDD	80	400	595	6	
19	Propranolol 2 mg/kg	360	545	VVI	125	320	485	33	Syncope†
20	Propranolol 120 mg	600	600	AAI	85	400	450	63	Sudden death‡
21		500	550	DDD	80	440	508	1	

*During follow-up the range of doses of beta-adrenergic blocking agents were 2 mg/kg to 120 mg/day for propranolol, 80 to 120 mg/day for nadolol and 100 to 200 mg/day for atenolol. †Pacemaker lead fracture: ‡After discontinuation of beta-blocker therapy. AAI = atrial demand pacing; AICD = automatic implantable cardioverter defibrillator; DDD = dual-chamber pacing; LCTS = left cervicothoracic sympathectomy; PMVT = polymorphous ventricular tachycardia; Pt = patient; VVI = ventricular demand pacemaker.

used because there is little experience with its use in patients with the long QT syndrome. Five of the nine also had unsuccessful left cervicothoracic sympathectomy.

The baseline range of the QT and QTc intervals was 440 to 640 ms (mean 517 ± 78) and 450 to 670 ms (mean 541 ± 62), respectively. After long-term pacing at 70 to 125 beats/min (mean 83 ± 12), the mean QT and QTc intervals decreased to 404 ± 37 and 479 ± 41 ms, respectively.

Follow-up. All patients but one were followed up for a minimum of 6 months (Table 2). The mean duration of follow-up for the group as a whole was 55 ± 45 months (range 1 to 156). Among patients who maintained both long-term beta-blocker therapy and consistent long-term pacing, only two had a cardiac event. In Patient 2, who was treated with an AAI pacemaker and had an unexplained syncopal episode during a casual telephone conversation, a dual-chamber pacemaker was inserted to exclude intermittent AV block. Because further evaluation with continuous ECG monitoring, tilt table testing, exercise treadmill testing and invasive electrophysiologic studies failed to pinpoint the cause of syncope, an interval defibrillator was inserted. This patient is currently without symptoms and has not had a defibrillator discharge during a 6-month follow-up interval. Patient 10 had recurrent episodes of polymorphous ventricular tachycardia and ventricular fibrillation (Fig. 1, A to C), and was initially treated with left cervicothoracic sympathectomy at another hospital. She remained free of arrhythmias for 48 h after operation but had an episode of polymorphous ventricular tachycardia similar to those that occurred preoperatively (Fig. 1D). Revision of her pacemaker to a dual-chamber unit resulted in prompt disappearance of the arrhythmias (Fig. 1E). She has had no symptoms on a regimen of beta-blockers, phenytoin and long-term dual-chamber pacing over a follow-up interval of approximately 6 months.

The remaining events occurred in three patients with lapses in combination therapy. Patient 20, with a history of multiple syncopal episodes, was successfully treated with combination therapy for 5 years. She subsequently joined a religious group that convinced her to discontinue drug therapy and she died suddenly 3 months later. Patients 3 and 19 had recurrences of the original symptoms related to pacemaker lead fracture. One of the leads was epicardial, implanted in a 3-month old baby; the other was an endocardial lead implanted in a 10-year old girl. The cause of symptoms was not documented in these patients but symptoms disappeared in both patients when effective pacing was reestablished.

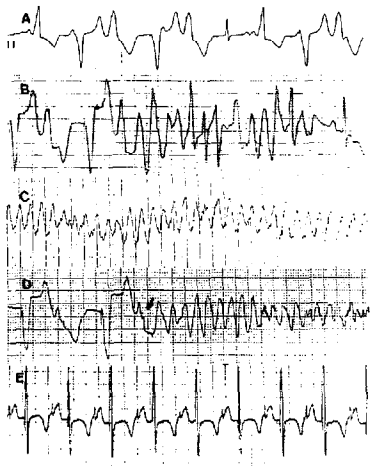

Figure 1. Patient 10. Electrocardiographic rhythm strips. **A**, Strip showing ventricular pacing in a ventricular demand (VVI) mode with ventricular bigeminy. The QT interval is prolonged for the paced complexes (500 ms) and the QTU interval is prolonged for one spontaneously conducted complex (beat 6). The premature ventricular complexes are not sensed by the pacemaker. **B**, Episode of spontaneous nonsustained polymorphous ventricular tachycardia that begins with a sequence of a paced beat followed by a ventricular premature beat practically identical to that in panel **A**. **C**, Episode of spontaneous polymorphous ventricular tachycardia that deteriorated into ventricular fibrillation and required direct current shock. **D**, Forty-eight hours after sympathectomy, an episode of spontaneous polymorphous ventricular tachycardia, beginning with a sequence very similar to that in panels **A** and **B**. The first premature complex is distorted by a pacemaker spike (**arrow**). The tachycardia deteriorated into ventricular fibrillation and required electrical shock. **E**, After sympathectomy and dual-chamber pacing, the QT interval is normal (360 ms).

Pacemaker problems. The prolonged cardiac refractory periods of these patients and the requirement to avoid pauses resulted in unique pacemaker problems. We abandoned AAI pacing for the reasons illustrated by Cases 12 and 19. In Patient 19 spontaneous 2:1 AV block developed after a premature ventricular depolarization (4). The compensatory pause after the premature ventricular depolarization resulted in prolongation of refractoriness, presumably at the level of the His bundle, and initiated episodes of 2:1 AV block. This type of response would not be avoided by using AAI pacing. Patient 12 had spontaneous episodes of AV Wenckebach block (particularly during sleep) that may have been in part related to the concomitant beta-blocker therapy.

Even the use of VVI or dual-chamber pacing has not obviated all problems. The relatively rapid pacing rates and the long ventricular effective refractory period require careful attention to programming variables, particularly with dual-chamber pacemakers as shown in the following cases. Pacemaker syndrome developed in Patient 9 after insertion of a DDD pacemaker. This case was previously reported (5) and will be briefly summarized. When the pacemaker was programmed to a lower rate of 85 beats/min and an AV delay of 250 ms (to shorten the QT interval and minimize ventricular pacing), episodic dyspnea and neck pulsations developed. Endocardial telemetry during a symptomatic episode showed retrograde ventriculoatrial conduction presumably initiated by a premature ventricular depolarization. The retrograde P wave resulted in atrial contraction against closed AV valves but was not sensed because it occurred within the pacemaker postventricular atrial refractory period. The next atrial stimulus failed to capture because of atrial refractoriness, and ventricular pacing occurred after an appropriately programmed AV delay and the cycle perpetuated itself. To maintain a heart rate necessary to normalize the QT interval, the AV delay was reprogrammed from 250 to 200 ms, which allowed for atrial capture by the atrial stimulus.

Another unique pacing problem was encountered in Patient 16, who underwent pacing at a rate of 80 beats/min in the AV mode. The routine 24-h ambulatory ECG recordings showed episodic prolonged pauses that were terminated by conducted sinus complexes (Fig. 2A). T wave oversensing was suspected but endocardial telemetry from the right ventricular lead revealed episodic potentials that occurred after completion of the T waves (Fig. 2B). These potentials were sensed by the ventricular lead and delayed the next atrial stimulus, which resulted in the pauses. This problem could be solved either by AV pacing at a rate of 100 beats/min (which resulted in loss of these potentials (Fig. 2C) or by pacing in the AAI mode at a rate of 80 beats/min. This patient showed no evidence of a lead problem as reflected by multiple random potentials or by 60-Hz noise, and impedance of the ventricular lead was normal. The potentials were thought to be possibly related to early afterdepolarizations that at slower rates achieved an amplitude sensed by the ventricular lead. The pacemaker was programmed to the AAI mode and the patient has had no symptoms during a follow-up period of 2 months.

Patient 19 underwent pacing in the VVI mode at a set rate of 120 beats/min with a long programmed ventricular refractory period of 325 ms designed to avoid T wave sensing. The patient developed seizures, and the monitoring strip showed sinus tachycardia at a rate of 214 beats/min with conducted beats that fell inside the pacemaker ventricular refractory period, allowing for the subsequent ventricular stimulus to fall on the T wave and trigger short episodes of nonsustained ventricular tachycardia (Fig. 3A). The problem was cor-

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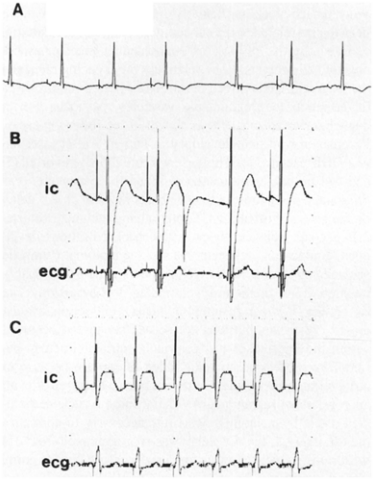


Figure 2. Patient 16. **A**, Electrocardiographic (ECG) rhythm strip showing atrial pacing and ventricular capture. A pause follows the fourth complex and is terminated by an escape sinus complex. The escape complex is characterized by atrial and ventricular events not sensed by the pacemaker. The observed ventriculoarterial intervals suggests that the pause was due to a sensed ventricular event occurring *after* the preceding T wave. **B**, Simultaneous recording of telemetered bipolar ventricular intracardiac electrogram (ic) and surface ECG lead showing that the pause is preceded by a large intracardiac potential occurring after inscription of the T wave. (Intracardiac electrogram gain 10 mV/division, paper speed 25 mm/s.) **C**, Recordings as in **B**. The atrial paced rate was increased to 100 beats/min, which resulted in the disappearance of the intracardiac potential and pauses in both bipolar and unipolar recording modes. (Gain 20 mV/division, paper speed 25 mm/s.)

rected by shortening the refractory period to 280 ms (Fig. 3B).

Value of dual therapy. The importance of dual therapy with beta-blockers and cardiac pacing is well illustrated by the three patients who had recurrent symptoms with either cessation of drug treatment or pacemaker malfunction, and particularly by Patient 19 (4). This patient presented in utero with irregular heart rate, and incessant episodes of polymorphous ventricular tachycardia were noted on day 1 (Fig. 4A). She was treated with oral propranolol without beneficial effect and required frequent cardioversions. Polymorphous ventricular tachycardia was related to episodes of functional 2:1 AV block. Ventricular overdrive pacing at a rate of 150 beats/min immediately eliminated all episodes of polymorphous ventricular tachycardia (Fig. 4B).

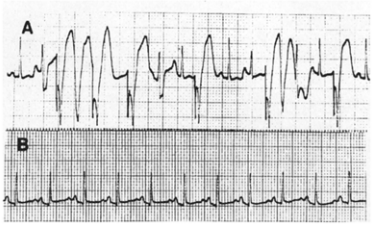
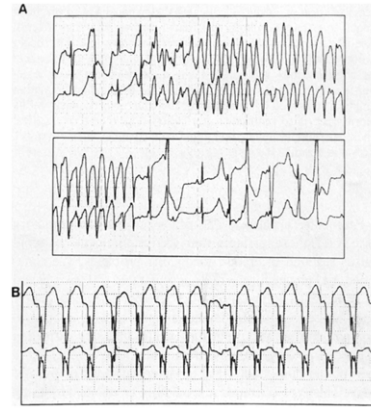


Figure 3. Patient 19. **A**, Electrocardiographic (ECG) rhythm strip showing sinus tachycardia (rate 214 beats/min) with phasic aberrancy and undersensing resulting in a ventricular spike falling on the T wave and sometimes producing short bursts of nonsustained monomorphic ventricular tachycardia. **B**, ECG strip showing sinus rhythm with normal sensing after the ventricular effective refractory period was shortened to 280 ms.

Patient 13, the daughter of Patient 4, is of particular interest. All family members were screened, and two of her brothers were found to have QT prolongation and were

Figure 4. Patient 19. **A, Top and middle panel of dual-channel Holter** ambulatory electrocardiographic recording showing an episode of ventricular bigeminy preceding an episode of polymorphous ventricular tachycardia that spontaneously terminates. Episodes of polymorphous ventricular tachycardia occurred despite beta-blocker therapy. Reproduced, by permission, from Van Hare et al. (4). **B**, After ventricular pacing in the VVI mode at 150 beats/min, showing normalization of the QT interval and disappearance of the polymorphous ventricular tachycardia.



treated with beta-blockers. Because Patient 13 was asymptomatic with normal serial ECG findings, it was decided not to treat her. While at school, she had a cardiac arrest due to documented ventricular fibrillation and was successfully resuscitated. Results of her echocardiogram, tilt table test, exercise treadmill test and invasive electrophysiologic study were normal. She was treated with a dual-chamber pacemaker and a beta-blocker and has remained asymptomatic during a follow-up interval of 22 months.

Discussion

Prior experience. Patients with the idiopathic long QT syndrome are at high risk for sudden cardiac death. Recognized high risk factors include a family history of sudden death and a history of syncope (6). Although beta-blocker therapy has been shown to be effective, it has limitations when used alone, as recently described in data collected from an international registry (6–9). Of 250 patients with the long QT syndrome treated with beta-blockers alone, 6% died suddenly and approximately 20% had recurrent syncope (6–9). Left cervicothoracic sympathectomy involving resection of the lower portion of the left stellate ganglion together with the first five to six thoracic ganglia has been suggested as an alternative therapeutic approach (6). A recent report from the worldwide registry documented the efficacy of sympathectomy in drug-resistant patients but also showed a 45% incidence rate of recurrent cardiac events over an approximately 6-year follow-up period (10). These events, which included sudden death (80% incidence rate) and aborted sudden death, occurred despite continuation of beta-blocker therapy in 84% of patients who underwent sympathectomy.

Results of combination therapy. In 1987, we (2) introduced the concept of combination beta-blocker therapy and cardiac pacing for all patients with the long QT syndrome. The rationale for this approach was prevention of either pauses or increased adrenergic tone that might trigger episodes of polymorphous ventricular tachycardia. In this study, we describe a relatively long-term follow-up in a sizable group of high risk patients. It is difficult to compare our patients with those in prior reports; however, their characteristics appeared to fit those of a relatively high risk group. For example, 18 (86%) of the 21 patients had syncope, 8 (38%) had been resuscitated from an episode of sudden cardiac death, 11 (52%) had a family history of sudden cardiac death or recurrent syncope, and 9 had not responded to a trial of beta-blockers with (5 patients) or without left cervicothoracic sympathectomy.

Complications. Despite the apparent high risk, none of the patients who adhered to the recommended combination therapy died suddenly. The only sudden death occurred in a patient who discontinued the use of beta-blockers. Of major concern were two patients (10%) who experienced recurrent syncope while receiving combination therapy. One (Patient 2) had an AAI pacemaker, and we cannot exclude the possibility of a pause-triggered event. The other (Patient 10) had documented polymorphous ventricular tachycardia despite a properly functioning VVI pacemaker and maximally tolerated beta-blocker therapy. This patient showed a persistent bigeminal rhythm that preceded the tachycardia episodes. A prolonged episode of polymorphous ventricular tachycardia that deteriorated into ventricular fibrillation was documented after sympathectomy. For reasons that are not clear, the patient's condition finally stabilized after the use of dual-chamber pacing and the addition of diphenylhydantoin therapy. One striking finding was the relation of bigeminy to polymorphous ventricular tachycardia. Although the mean heart rate was more rapid during bigeminy than that recorded during dual-chamber pacing, polymorphous ventricular tachycardia disappeared after the disappearance of premature ventricular complexes. This finding suggests that the short-long sequences induced by premature ventricular complexes may trigger polymorphous ventricular tachycardia. One possible mechanism may involve the induction of afterdepolarization as a result of either increased intracellular calcium concentration after the premature complex (11) or direct mechanical stress and stretch (12) produced by the extrasystolic beat. The findings in these two patients suggest that factors apart from prolonged pauses or enhanced beta-adrenergic tone might trigger polymorphous ventricular tachycardia. Other investigators (13–15), for example, have suggested the possible role of alpha-receptor stimulation in provoking arrhythmias in these patients.

Previous studies. A recent report by Moss et al. (16) described the beneficial effects of combination therapy for 30 patients with the long QT syndrome enrolled in a voluntary registry. They described recurrent symptoms in 9 of 30 patients. The difference in recurrence rate between studies may be due to differences in the paced rate used. In our study, the minimal paced rate needed to normalize the QT interval was used. In the study of Moss et al., the paced rate was known in 19 patients (69 ± 8 beats/min in 6 patients with cardiac events and 75 ± 11 beats/min in 13 without events) and was associated with normalization of the QT interval in 10 patients. In addition, the causes of symptomatic recurrences were not defined and the issue of possible pacemaker malfunction was not addressed. It is conceivable that the higher incidence of adverse effects noted in the study by Moss et al. was conceivably due either to failure to normalize the QT interval with pacing or to pacemaker malfunction in some patients, or to both. Similar considerations apply to a case report by Case and Gillette (17) of a child who did not respond to pacemaker therapy.

Pacemaker problems. The inadequacy of isolated atrial pacing was appreciated relatively early in our experience. In five patients, spontaneous or induced episodes of AV block were recorded and the block was documented to be infra-Hisian in four, including two siblings (Patients 3 and 21). Previous studies from our laboratory and others (6,17–20) have documented the functional nature of this block, which may be initiated, for example, by a compensatory pause

after a premature ventricular depolarization resulting in increased refractoriness of the His-Purkinje system. Once block occurs, it tends to be perpetuated by the pause produced by AV block (3). In addition, we noted spontaneous episodes of Mobitz type I AV block in one patient. The incidence of AV block would be expected to be increased in patients treated with large doses of beta-blockers. In view of these findings, our preference is to use dual-chamber pacemakers in adults with the long QT syndrome.

The unique requirements for the maintenance of a specific rate for QT normalization in patients with prolonged refractory periods produce interesting pacemaker problems. For example, maintenance of a critical rate and provision for adequate AV delay to allow intrinsic AV conduction resulted in a pacemaker syndrome in Patient 9. In this patient, retrograde atrial depolarization fell in the atrial refractory period and the atrium was refractory to the subsequent paced atrial event (4).

Other significant problems may relate to sensing of T and U waves, which may be abnormal in these patients (2). TU wave and pacemaker stimulus afterpotential oversensing have to be avoided to prevent pauses that may potentially trigger episodes of polymorphous ventricular tachycardia and may require programming of relatively long refractory periods. In one patient, sinus complexes during sinus tachycardia were not sensed because of a long programmed refractory period, and bursts of nonsustained ventricular tachycardia resulted when pacemaker spikes fell on the T wave (Fig. 3). The problem could be resolved in this patient by shortening the refractory period. Oversensing proved to be a problem in one patient (Patient 16) in whom intracardiac telemetry showed a very large potential after the T wave, which was sensed and led to pauses (Fig. 2). The cause of this unusual potential is not clear. It could represent "noise" due to lead fracture or insulation break. However, there was no other indication of a lead problem. Some screw-in leads may cause artifactual potentials probably due to intermittent contact between the screw and the ring cathode (21). In this patient, deep breathing and rapid heart rates neither changed nor accentuated the potentials. Another possible explanation is that they represent local abnormal afterdepolarizations. However, their huge amplitude, inconstant relation to the previous QRS complex and lack of constant relation to heart rate do not favor this explanation. Whatever the mechanism, oversensing should be corrected to avoid pause-dependent arrhythmia. This case underlines the importance of lead telemetry for identifying the mechanism of oversensing.

Findings in family members. Another interesting observation emerged from our study. An asymptomatic family member with serial ECGs showing normal QT and QTc intervals had an episode of sudden cardiac arrest, suggesting that apparently unaffected siblings are still at risk. Cardiac symptoms in unaffected members of a family with the long QT syndrome have been previously reported (6,22), but we are unaware of prior reports of aborted sudden cardiac death in asymptomatic siblings with a normal QT interval.

Limitations. Some patients had a relatively short follow-up interval, which poses difficulties in assessing the impact of combination therapy. Two patients (Patients 9 and 10) had only one episode of syncope before they were given combination therapy, whereas one patient (Patient 21) was asymptomatic and had a short (1-month) follow-up period. However, Patient 10 had documented polymorphic ventricular tachycardia before and after left cervicothoracic sympathectomy and remains asymptomatic after combination therapy.

Although all of our patients received combination therapy, the possibility that either treatment alone might have sufficed cannot be excluded. The reappearance of symptoms on discontinuation of either pacing (Patients 3 and 19) or beta-blockers (Patient 20) supports the hypothesis that both components are important but does not prove it. For example, Patient 20, who had an AAI pacemaker, may not have responded to treatment because of intermittent AV block that triggered polymorphous ventricular tachycardia.

Conclusions. Over a follow-up interval of 55 months, none of the patients who had long-term combination therapy had sudden cardiac death. This therapy is not without risk because two of these patients (10%) did experience recurrent syncope and one had documented polymorphous ventricular tachycardia. Three other patients experienced recurrence of symptoms related to pacemaker malfunction. These results provide long-term data on combination therapy and appear to compare favorably with results obtained with beta blockers used alone or in addition to sympathectomy. Moreover, in patients with the long QT syndrome who are deemed candidates for an internal defibrillator, the combination of beta-blockers and long-term pacing is recommended to decrease the number of defibrillator discharges.

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